

## INVENTOR SEARCH

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L8 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:554455 HCAPLUS Full-text

DOCUMENT NUMBER: 143:318687

TITLE: 4-Hydroxy-oxyphenbutazone is a potent inhibitor of cytokine production

AUTHOR(S): Ten Brinke, Anja; Dekkers, David W. C.; Notten, Silla M.; Karsten, Miriam L.; de Groot, Els R.; Aarden, Lucien A.

CORPORATE SOURCE: Department of Immunopathology, Sanquin Research at CLB, Amsterdam, 1006 AD, Neth.

SOURCE: European Cytokine Network (2005), 16(2), 144-151  
CODEN: ECYNEJ; ISSN: 1148-5493

PUBLISHER: John Libbey Eurotext

DOCUMENT TYPE: Journal

LANGUAGE: English

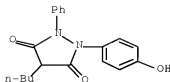
AB 4-Hydroxy-oxyphenbutazone (4OH-OPB), is currently in phase II trials for its immunosuppressive effect in patients with rheumatoid arthritis. 4OH-OPB and other compds. related to phenylbutazone were tested for their effect on in vitro cytokine production by monocytes and lymphocytes present in peripheral mononuclear cells (PBMC) or whole blood (WB) cultures, and compared against phenylbutazone and oxyphenbutazone, two known anti-inflammatory drugs. In PBMC cultures, 4OH-OPB was by far the most potent inhibitor, and both monokines and Th1 and Th2 lymphokines were efficiently inhibited at low concns. In WB cultures, 4OH-OPB was less effective than in PBMC cultures, but was still the best inhibitor of lymphokine production and, furthermore, was the only inhibitor of monokine production. The increase in 4OH-OPB concentration needed to induce the same inhibition of cytokine production in WB as in PBMC culture could be mimicked by the addition of erythrocytes to the PBMC cultures. Expts. with radioactively-labeled 4OH-OPB suggest that 4OH-OPB is taken up very rapidly into erythrocytes and is secreted by the erythrocytes with much slower kinetics via a multidrug-resistance-associated protein. The secreted compound is most likely structurally different from 4OH-OPB, as in PBMC and WB cultures, the inhibition of cytokine production seems to be caused by a different mechanism. In PBMC cultures, the inhibition of cytokine production is accompanied by a loss of cell viability, while this is not the case when 4OH-OPB inhibits cytokine production in WB. Our data suggest that 4OH-OPB may be useful as an immunosuppressive drug for patients with inflammatory diseases.

IT 129-20-4, Oxyphenbutazone

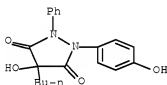
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(hydroxyoxyphenbutazone is a potent inhibitor of cytokine production)

RN 129-20-4 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)



IT 55648-39-0, 4-Hydroxy-oxyphenbutazone  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (hydroxyoxyphenbutazone is a potent inhibitor of cytokine  
 production)  
 RN 55648-39-0 HCAPLUS  
 CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
 (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
 (1 CITINGS)  
 REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2010 ACS ON STN  
 ACCESSION NUMBER: 2005:120731 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:219277

TITLE: A preparation of glutathione-substituted  
 phenbutazone derivatives, useful as  
 antiinflammatory, antiviral, and immunomodulatory  
 agents

INVENTOR(S): Dekkers, David Walterus Cornelis;  
 Aarden, Lucien Adrianus; Ten Brink, Janna  
 Alberdina

PATENT ASSIGNEE(S): A-Viral Asa, Norway; Cockbain, Julian

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

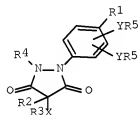
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011679	A1	20050210	WO 2004-GB3210	20040723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

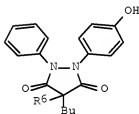
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 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

CA 2533506	A1	20050210	CA 2004-2533506	20040723
EP 1651212	A1	20060503	EP 2004-743541	20040723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006528165	T	20061214	JP 2006-520903	20040723
US 20070155812	A1	20070705	US 2006-565507	20061002
PRIORITY APPLN. INFO.:			GB 2003-17269	A 20030723
			WO 2004-GB3210	W 20040723

OTHER SOURCE(S): CASREACT 142:219277; MARPAT 142:219277  
 GI



I



II

AB The invention relates to a preparation of glutathione-substituted phenbutazone derivs. of formula I [wherein: R1 is O or S; R2 is H or C1-C10 organic group attached by a carbon atom; X is H, O, -O-O-, S, or -S-S-; R3 is absent when X = H, or R3 is H, OH, or thiol protecting group; R4 is (un)substituted hetero- or homocyclic aryl group; one Y group is S and the other is either H (in which case only one R5 is present) or S; R5 is an organic group of mol. weight up to around 500 amu], useful as antiinflammatory, antiviral, and immunomodulatory agents. For instance, phenbutazone derivative II (R6 = OH) was prepared via hydroxylation of II (R6 = H) in the presence of H2O2 with a yield of 35%.

BIOL. tests indicated that 0.5-5.0  $\mu$ M of di-glutathione-substituted phenbutazone derivative II (R6 = OH) was sufficient to completely block production of the cytokines IL6 and granulocyte colony-stimulating factor.

IT 842163-84-2P 842163-85-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of glutathione-substituted phenbutazone derivs.

useful as antiinflammatory, antiviral, and immunomodulatory agents)

RN 842163-84-2 HCAPLUS

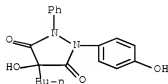
CN Glycine, L- $\gamma$ -glutamyl-L-cysteinyl-, compd. with

4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione (1:1)  
(9CI) (CA INDEX NAME)

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CRN 55648-39-0

CMF C19 H20 N2 O4

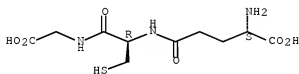


CM 2

CRN 70-18-8

CMF C10 H17 N3 O6 S

Absolute stereochemistry.



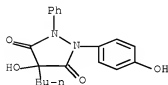
RN 842163-85-3 HCAPLUS

CN Glycine, L-gamma-glutamyl-L-cysteinyl-, compd. with  
4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione (2:1)  
(9CI) (CA INDEX NAME)

CM 1

CRN 55648-39-0

CMF C19 H20 N2 O4

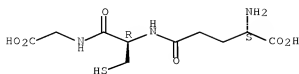


CM 2

CRN 70-18-8

CMF C10 H17 N3 O6 S

Absolute stereochemistry.



IT 70-18-8, Glutathione, reactions 129-20-4

RL: RCT (Reactant); RACT (Reactant or reagent)

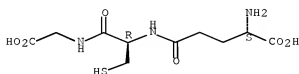
(preparation of glutathione-substituted phenbutazone derivs.

useful as antiinflammatory, antiviral, and immunomodulatory agents)

RN 70-18-8 HCAPLUS

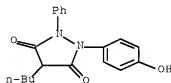
CN Glycine, L-γ-glutamyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 129-20-4 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)



IT 55648-39-0P

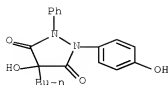
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of glutathione-substituted phenbutazone derivs.

useful as antiinflammatory, antiviral, and immunomodulatory agents)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2010 ACS ON STN

ACCESSION NUMBER: 2005:120721 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:219275

TITLE: A preparation of quinonimine derivatives, useful as  
antiallergy, anti-inflammatory, and antiviral agents

INVENTOR(S): Dekkers, David Walterus Cornelis;  
Aarden, Lucien Adrianus; Ten Brink, Janna  
Alberdina

PATENT ASSIGNEE(S): A-Viral Asa, Norway; Cockbain, Julian

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

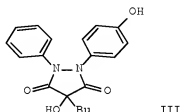
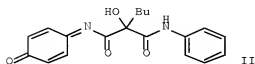
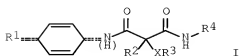
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO 2005011664	A1	20050210	WO 2004-GB3189	20040723
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2533504	A1	20050210	CA 2004-2533504	20040723
EP 1651203	A1	20060503	EP 2004-743521	20040723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006528164	T	20061214	JP 2006-520899	20040723
US 20070112072	A1	20070517	US 2006-565506	20061002
PRIORITY APPLN. INFO.:			GB 2003-17268	A 20030723
			WO 2004-GB3189	W 20040723

OTHER SOURCE(S): CASREACT 142:219275; MARPAT 142:219275

GI



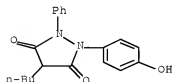
AB The invention relates to a preparation of quinonimine derivs. of formula I [wherein: R1 is O or S when double bonded to the ring, or R1 is OH, SH, or a protected equivalent when single bonded to the ring; R2 is H or more preferably an organic group attached by a carbon atom; X is H, O, -O-O-, or S, etc.; R3 is absent when X = H, or R3 is H, OH, or SH, etc.; R4 is a (un)substituted hetero- or preferably homo-cyclic aryl group; and groups T1 are independently absent, H, or S-R5; R5 is an organic group of mol. weight up to around 500 amu], useful as antiallergy, anti-inflammatory, and antiviral agents. For instance, quinonimine derivative II was prepared via ring-opening of 4-hydroxy-oxyphenbutazone (III). Biol. tests showed that 0.5 - 2  $\mu$ M of II was sufficient to completely block production of cytokines IL6 and granulocyte colony-stimulating factor.

IT 129-20-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of quinonimine derivs. useful as antiallergy,  
anti-inflammatory, and antiviral agents)

RN 129-20-4 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)



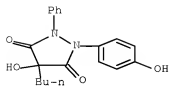
IT 55648-39-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of quinonimine derivs. useful as antiallergy,  
anti-inflammatory, and antiviral agents)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-

(CA INDEX NAME)



REFERENCE COUNT:

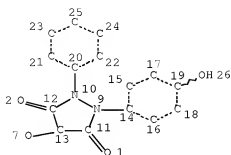
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THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



## RESULTS FROM SEARCHES IN REGISTRY AND CAPLUS

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L9 STR



NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE  
L11 7 SEA FILE=REGISTRY SSS FUL L9  
L12 11 SEA FILE=HCAPLUS ABB=ON L11

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L12 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2005:1218491 HCAPLUS Full-text  
DOCUMENT NUMBER: 143:472599  
TITLE: Method of tonic treatment with oxypentenbutazone derivatives  
INVENTOR(S): Joergen, Karlsten  
PATENT ASSIGNEE(S): A-Viral Asa, Norway; Goddard, Chris  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005107748	A2	20051117	WO 2005-GB1772	20050510
WO 2005107748	A3	20061102		

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 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

CA 2566228 A1 20051117 CA 2005-2566228 20050510  
 EP 1750692 A2 20070214 EP 2005-742434 20050510  
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 IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,  
 HR, LV, MK, YU

JP 2007537221 T 20071220 JP 2007-512329 20050510  
 US 20080262068 A1 20081023 US 2006-596278 20061113

PRIORITY APPLN. INFO.: NO 2004-1947 A 20040512  
 WO 2005-GB1772 W 20050510

## ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

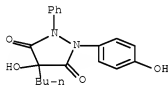
OTHER SOURCE(S): MARPAT 143:472599

AB The present invention provides a method of tonic treatment of an aging  
 mammalian subject, or a subject suffering from mild inflammation, lupus,  
 fatigue, lethargy or the after-effects of infection, disease or treatment,  
 comprising administration of oxyphenbutazone derivative or a salt thereof.

IT 55648-39-0P, 4-Hydroxyoxyphenbutazone  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (treatment with oxyphenbutazone derivs. diseases of old age)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
 (CA INDEX NAME)

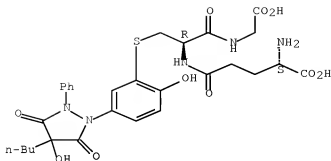


IT 869463-29-6P 869463-30-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (treatment with oxyphenbutazone derivs. diseases of old age)

RN 869463-29-6 HCAPLUS

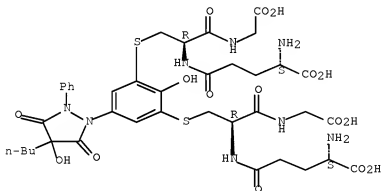
CN Glycine, L-γ-glutamyl-S-[5-(4-butyl-4-hydroxy-3,5-dioxo-2-phenyl-1-  
 pyrazolidinyl)-2-hydroxyphenyl]-L-cysteinyl- (SCI) (CA INDEX NAME)

Absolute stereochemistry.



RN 869463-30-9 HCAPLUS  
 CN Glycine, 2,2'-[5-(4-butyl-4-hydroxy-3,5-dioxo-2-phenyl-1-pyrazolidinyl)-2-hydroxy-1,3-phenylene]bis[L-glyutamyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2005:554455 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 143:318687  
 TITLE: 4-Hydroxy-oxyphenbutazone is a potent inhibitor of cytokine production  
 AUTHOR(S): Ten Brinke, Anja; Dekkers, David W. C.; Notten, Silla M.; Karsten, Miriam L.; de Groot, Els R.; Aarden, Lucien A.  
 CORPORATE SOURCE: Department of Immunopathology, Sanquin Research at CLB, Amsterdam, 1006 AD, Neth.  
 SOURCE: European Cytokine Network (2005), 16(2), 144-151  
 CODEN: ECYNEJ; ISSN: 1148-5493  
 PUBLISHER: John Libbey Eurotext  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 4-Hydroxy-oxyphenbutazone (4OH-OPB), is currently in phase II trials for its immunosuppressive effect in patients with rheumatoid arthritis. 4OH-OPB and other compds. related to phenylbutazone were tested for their effect on in

vitro cytokine production by monocytes and lymphocytes present in peripheral mononuclear cells (PBMC) or whole blood (WB) cultures, and compared against phenylbutazone and oxyphenbutazone, two known anti-inflammatory drugs. In PBMC cultures, 4OH-OPB was by far the most potent inhibitor, and both monokines and Th1 and Th2 lymphokines were efficiently inhibited at low concns. In WB cultures, 4OH-OPB was less effective than in PBMC cultures, but was still the best inhibitor of lymphokine production and, furthermore, was the only inhibitor of monokine production. The increase in 4OH-OPB concentration needed to induce the same inhibition of cytokine production in WB as in PBMC culture could be mimicked by the addition of erythrocytes to the PBMC cultures. Expts. with radioactively-labeled 4OH-OPB suggest that 4OH-OPB is taken up very rapidly into erythrocytes and is secreted by the erythrocytes with much slower kinetics via a multidrug-resistance-associated protein. The secreted compound is most likely structurally different from 4OH-OPB, as in PBMC and WB cultures, the inhibition of cytokine production seems to be caused by a different mechanism. In PBMC cultures, the inhibition of cytokine production is accompanied by a loss of cell viability, while this is not the case when 4OH-OPB inhibits cytokine production in WB. Our data suggest that 4OH-OPB may be useful as an immunosuppressive drug for patients with inflammatory diseases.

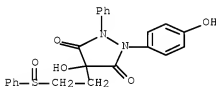
IT 865484-62-4

RL: PAC (Pharmacological activity); BIOL (Biological study)

(hydroxyoxyphenbutazone is a potent inhibitor of cytokine production)

RN 865484-62-4 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-4-[2-(phenylsulfinyl)ethyl]- (CA INDEX NAME)



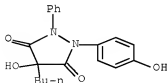
IT 55648-39-0, 4-Hydroxy-oxyphenbutazone

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydroxyoxyphenbutazone is a potent inhibitor of cytokine production)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)

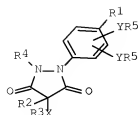


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

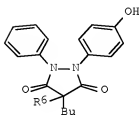
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2005:120731 HCAPLUS Full-text  
 DOCUMENT NUMBER: 142:219277  
 TITLE: A preparation of glutathione-substituted phenbutazone derivatives, useful as antiinflammatory, antiviral, and immunomodulatory agents  
 INVENTOR(S): Dekkers, David Walterus Cornelis; Aarden, Lucien Adrianus; Ten Brink, Janna Alberdina  
 PATENT ASSIGNEE(S): A-Viral Asa, Norway; Cockbain, Julian  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011679	A1	20050210	WO 2004-GB3210	20040723
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2533506	A1	20050210	CA 2004-2533506	20040723
EP 1651212	A1	20060503	EP 2004-743541	20040723
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
JP 2006528165	T	20061214	JP 2006-520903	20040723
US 20070155812	A1	20070705	US 2006-565507	20061002
PRIORITY APPLN. INFO.:			GB 2003-17269	A 20030723
			WO 2004-GB3210	W 20040723
OTHER SOURCE(S):		CASREACT 142:219277; MARPAT 142:219277		
GI				



I



II

AB The invention relates to a preparation of glutathione-substituted phenbutazone derivs. of formula I [wherein: R1 is O or S; R2 is H or C1-C10 organic group attached by a carbon atom; X is H, O, -O-O-, S, or -S-S-; R3 is absent when X = H, or R3 is H, OH, or thiol protecting group; R4 is (un)substituted hetero- or homocyclic aryl group; one Y group is S and the other is either H (in which case only one R5 is present) or S; R5 is an organic group of mol. weight up to around 500 amu], useful as antiinflammatory, antiviral, and immunomodulatory agents. For instance, phenbutazone derivative II (R6 = OH) was prepared via hydroxylation of II (R6 = H) in the presence of H2O2 with a yield of 35%.

Biol. tests indicated that 0.5-5.0  $\mu$ M of di-glutathione-substituted phenbutazone derivative II (R6 = OH) was sufficient to completely block production of the cytokines IL6 and granulocyte colony-stimulating factor.

IT 842163-84-2P 842163-85-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of glutathione-substituted phenbutazone derivs. useful as antiinflammatory, antiviral, and immunomodulatory agents)

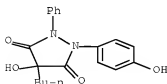
RN 842163-84-2 HCAPLUS

CN Glycine, L- $\gamma$ -glutamyl-L-cysteinyl-, compd. with 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 55648-39-0

CMF C19 H20 N2 O4

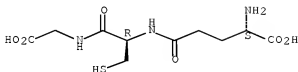


CM 2

CRN 70-18-8

CMF C10 H17 N3 O6 S

Absolute stereochemistry.



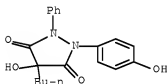
RN 842163-85-3 HCAPLUS

CN Glycine, L-γ-glutamyl-L-cysteinyl-, compd. with  
 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione (2:1)  
 (9CI) (CA INDEX NAME)

CM 1

CRN 55648-39-0

CMF C19 H20 N2 O4

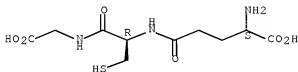


CM 2

CRN 70-18-8

CMF C10 H17 N3 O6 S

Absolute stereochemistry.

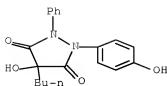


IT 55648-39-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of glutathione-substituted phenbutazone derivs. useful as  
 antiinflammatory, antiviral, and immunomodulatory agents)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
 (CA INDEX NAME)

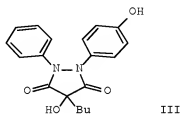
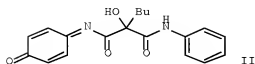
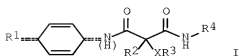


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2005:120721 HCAPLUS Full-text  
DOCUMENT NUMBER: 142:219275  
TITLE: A preparation of quinonimine derivatives, useful as  
antiallergy, anti-inflammatory, and antiviral agents  
INVENTOR(S): Dekkers, David Walterus Cornelis; Aarden, Lucien  
Adrianus; Ten Brink, Janna Alberdina  
PATENT ASSIGNEE(S): A-Viral Asa, Norway; Cockbain, Julian  
SOURCE: PCT Int. Appl., 46 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011664	A1	20050210	WO 2004-GB3189	20040723
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2533504	A1	20050210	CA 2004-2533504	20040723
EP 1651203	A1	20060503	EP 2004-743521	20040723
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
JP 2006528164	T	20061214	JP 2006-520899	20040723
US 20070112072	A1	20070517	US 2006-565506	20061002
PRIORITY APPLN. INFO.:			GB 2003-17268	A 20030723
			WO 2004-GB3189	W 20040723
OTHER SOURCE(S):	CASREACT 142:219275; MARPAT 142:219275			
GI				





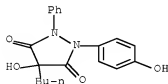
AB The invention relates to a preparation of quinonimine derivs. of formula I [wherein: R1 is O or S when double bonded to the ring, or R1 is OH, SH, or a protected equivalent when single bonded to the ring; R2 is H or more preferably an organic group attached by a carbon atom; X is H, O, -O-O-, or S, etc.; R3 is absent when X = H, or R3 is H, OH, or SH, etc.; R4 is a (un)substituted hetero- or preferably homo-cyclic aryl group; and groups T1 are independently absent, H, or S-R5; R5 is an organic group of mol. weight up to around 500 amu], useful as antiallergy, anti-inflammatory, and antiviral agents. For instance, quinonimine derivative II was prepared via ring-opening of 4-hydroxy-oxyphenbutazone (III). Biol. tests showed that 0.5 - 2  $\mu\text{M}$  of II was sufficient to completely block production of cytokines IL6 and granulocyte colony-stimulating factor.

IT 55648-39-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of quinonimine derivs. useful as antiallergy, anti-inflammatory, and antiviral agents)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)

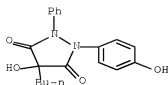


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2004:534311 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 141:65095

TITLE: Method for selection of compounds which inhibit clonal cell growth and use thereof  
 INVENTOR(S): Tjotta, Enok  
 PATENT ASSIGNEE(S): Norway  
 SOURCE: PCT Int. Appl., 222 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055175	A1	20040701	WO 2003-NO335	20031007
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
NO 326130	B1	20081006	NO 2002-4853	20021008
CA 2501039	A1	20040701	CA 2003-2501039	20031007
AU 2003302154	A1	20040709	AU 2003-302154	20031007
AU 2003302154	B2	20080612		
EP 1549742	A1	20050706	EP 2003-811277	20031007
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
ZA 2005002609	A	20060726	ZA 2005-2609	20050331
US 20060121449	A1	20060608	US 2005-530488	20050406
PRIORITY APPLN. INFO.:			NO 2002-4853	A 20021008
			WO 2003-NO335	W 20031007
AB	A three step method for selection and testing of compds. inhibiting clonal cell growth is disclosed. Method involves: 1) screening for substances that inhibit clonal growth in a culture, 2) in the same culture, testing whether a high local cell concentration (collocation) will decrease the inhibiting effect of such substances on clonal cell growth and 3) testing if export of metastatic cells from a tumor site could be locked by such substances. It should then be possible to decrease or even abolish the development of malignant disease or metastasis from primary tumors and development of benign tumors including atheromas in arteries. The method may also detect compds. that increase clonal growth. These compds. might possess carcinogenic properties or could be used for stimulation of a failing immune system.			
IT	55648-39-0 RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (method for selection of compds. which inhibit clonal cell growth and use thereof)			
RN	55648-39-0 HCAPLUS			
CN	3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl- (CA INDEX NAME)			



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
ACCESSION NUMBER: 2001:12423 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 134:86239  
TITLE: Preparation of pyrazolidinol compounds as anti-HIV  
agents  
INVENTOR(S): Tjotta, Enok; Klaveness, Jo  
PATENT ASSIGNEE(S): A-Viral AS, Norway; Cockbain, Julian  
SOURCE: PCT Int. Appl., 39 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000585	A1	20010104	WO 2000-GB2513	20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377200	A1	20010104	CA 2000-2377200	20000629
EP 1194409	A1	20020410	EP 2000-940667	20000629
EP 1194409	B1	20060201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
JP 2003503389	T	20030128	JP 2001-506995	20000629
AU 775355	B2	20040729	AU 2000-55575	20000629
AT 316960	T	20060215	AT 2000-940667	20000629
ZA 2002000432	A	20030117	ZA 2002-432	20020117
US 6852749	B1	20050208	US 2002-19229	20020529
US 20040152751	A1	20040805	US 2003-701498	20031106
US 20070037772	A1	20070215	US 2006-371226	20060309
US 20080287390	A1	20081120	US 2008-7694	20080114
PRIORITY APPLN. INFO.:			GB 1999-15184	A 19990629
			WO 2000-GB2513	W 20000629
			US 2002-19229	A1 20020529
			US 2003-701498	B1 20031106
			US 2006-371226	B1 20060309

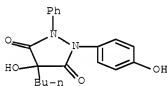
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides the use of an optionally hydroxy-protected 4-hydroxy or hydroperoxy-3,5-dioxypyrazolidine or an equivalent wherein a pyrazolidine ring attached oxygen is replaced by a sulfur as anti-HIV agents. Addnl., the invention provides a method of combating HIV infection which comprises administering to an HIV-infected patient a T-lymphocyte growth suppressing agent, preferably a pyrazolidinol. E.g., 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione was prepared

IT 55648-39-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of pyrazolidinol compds. as anti-HIV agents)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
 (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
 (4 CITINGS)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1986:412218 HCAPLUS Full-text

DOCUMENT NUMBER: 105:12218

ORIGINAL REFERENCE NO.: 105:2041a,2044a

TITLE: Stability-indicating assay for oxyphenbutazone. Part  
 II. High-performance liquid chromatographic  
 determination of oxyphenbutazone and its degradation  
 products

AUTHOR(S): Fabre, Huguette; Ramiaramana, Andrianandrasana;

Blanchin, Marie Dominique; Mandrou, Bernadette

CORPORATE SOURCE: Lab. Chim. Anal., Fac. Pharm., Montpellier, 34060, Fr.

SOURCE: Analyst (Cambridge, United Kingdom) (1986), 111(2),

133-7

CODEN: ANALAO; ISSN: 0003-2654

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An HPLC method is proposed for the simultaneous determination of  
 oxyphenbutazone (I) [129-20-4] and 6 potential decomposition products, using  
 a reversed-phase column and UV detection. The method is more sensitive than  
 thin-layer chromatog. and allows the determination of 0.1% of each degradation  
 product (with respect to I). It was applied to the anal. of com. tablets,  
 capsules, and ointments.

IT 55648-39-0 101689-92-3

RL: ANT (Analyte); ANST (Analytical study)

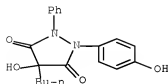
(determination of, in presence of oxyphenbutazone, in pharmaceuticals by

HPLC)

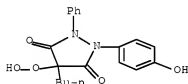
RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-

(CA INDEX NAME)



RN 101689-92-3 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroperoxy-1-(4-hydroxyphenyl)-2-phenyl-  
(CA INDEX NAME)OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)

L12 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1986:174743 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 104:174743

ORIGINAL REFERENCE NO.: 104:27569a,27572a

TITLE: Stability-indicating assay for oxyphenbutazone. Part  
I. Thin-layer chromatographic determination of  
oxyphenbutazone and its degradation products  
AUTHOR(S): Fabre, H.; Ramiarmanana, A.; Blanchin, M. D.;  
Mandrou, B.CORPORATE SOURCE: Lab. Chim. Anal., Fac. Pharm., Montpellier, 34060, Fr.  
SOURCE: Analyst (Cambridge, United Kingdom) (1985), 110(11),  
1289-93

CODEN: ANALAQ; ISSN: 0003-2654

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A high-performance TLC procedure for the separation and determination of  
oxyphenbutazone (I) [129-20-4] and its 6 main potential degradation products  
in situ is reported. The method avoids degradation of I in situ by chelating  
Fe in the silica plate and allows the simultaneous assay of I and its  
decomposition products using a chromatog. spectrophotometer. The method was  
validated as a stability-indicating assay of I in tablets and capsules. It  
allows the determination of 0.5% decomposition products (with respect to I).  
In the formulations analyzed, only trace amts. of 2 oxidation products were  
found.

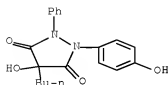
IT 55648-39-0 101689-92-3

RL: ANT (Analyte); ANST (Analytical study)

(determination of, as oxyphenbutazone degradation product in  
pharmaceuticals,  
high-performance TLC)

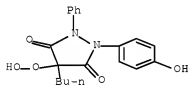
RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
(CA INDEX NAME)



RN 101689-92-3 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroperoxy-1-(4-hydroxyphenyl)-2-phenyl-  
(CA INDEX NAME)



L12 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1985:400129 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 103:129

ORIGINAL REFERENCE NO.: 103:19a,22a

TITLE: Metabolism of phenylbutazone in rats

AUTHOR(S): Alexander, D. Mary; Mathew, G. E. A.; Wilson, Beverley J.

CORPORATE SOURCE: Dep. Pharm., Univ. Durban-Westville, Durban, 4000, S. Afr.

SOURCE: Xenobiotica (1985), 15(2), 123-8

CODEN: XENOBH; ISSN: 0049-8254

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The metabolism of phenylbutazone (I) [50-33-9] was investigated in female rats dosed with the drug by gavage. The major route of excretion is via the urine, with 50% of the dose being excreted in the 1st 24 h. A small percentage of the dose is excreted in the feces. Following administration of [<sup>14</sup>C]I, 5 labeled, unconjugated hydroxy compds. were identified in the urine by TLC and autoradiog.; both hydrolyzable and nonhydrolyzable conjugates were found. Aqueous exts. of feces contained O-conjugates of oxyphenbutazone and 4-hydroxyoxyphenbutazone (which may be a decomposition product). Urine metabolites soluble in organic solvents were quantified by inverse isotope dilution assay and spectrophotometric anal. The major metabolite is the  $\gamma$ -hydroxy derivative of phenylbutazone present both as the lactone [96740-75-9] and as the straight-chain compound [568-76-3], whereas oxyphenbutazone [129-20-4] and p, $\gamma$ -dihydroxyphenylbutazone [7720-49-2] are minor metabolites.

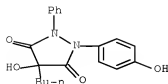
IT 55648-39-0D, O-conjugates

RL: BIOL (Biological study)  
(as phenylbutazone metabolite)

RN 55648-39-0 HCAPLUS

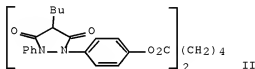
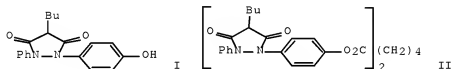
CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-

(CA INDEX NAME)



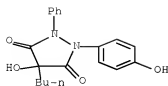
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD  
(2 CITINGS)

L12 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 1983:100887 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 98:100887  
 ORIGINAL REFERENCE NO.: 98:15225a,15228a  
 TITLE: Nonsteroidal antiinflammatory agents. 9. Local effect of oxyphenbutazone derivatives  
 AUTHOR(S): Rahtz, Dieter; Baettcher, Irmgard  
 CORPORATE SOURCE: Forschungslab., Shering A.-G., Berlin, 1000/65, Fed. Rep. Ger.  
 SOURCE: European Journal of Medicinal Chemistry (1982), 17(5), 429-32  
 CODEN: EJMCA5; ISSN: 0009-4374  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German  
 OTHER SOURCE(S): CASREACT 98:100887  
 GI



AB Lipophilic oxyphenbutazone (I) [129-20-4] esters were synthesized and tested for antiinflammatory activity in various inflammation model systems. Esterification of the phenolic OH of I with short- and long-chain fatty acids yielded monoesters with local antiinflammatory activity which was  $\leq$ I. However esterification of I with hexanedioic acid yielded a diester (II) [59530-06-2] which had a significantly more pronounced local antiinflammatory activity than I, but systemic antiinflammatory activity similar to that of I. The topical antiinflammatory activity of II was similar to that observed with hydrocortisone acetate in patients with eczema vulgare.

IT 55648-39-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 55648-39-0 HCAPLUS  
 CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
 (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD  
(3 CITINGS)

L12 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1975:453142 HCAPLUS Full-text

DOCUMENT NUMBER: 83:53142

ORIGINAL REFERENCE NO.: 83:8295a,8298a

TITLE: Oxidation of oxyphenbutazone by sheep vesicular gland microsomes and lipoxigenase

AUTHOR(S): Portoghese, Philip S.; Svanborg, Kerstin; Samuelsson, Bengt

CORPORATE SOURCE: Dep. Chem., Karolinska Inst., Stockholm, Swed.

SOURCE: Biochemical and Biophysical Research Communications (1975), 63(3), 748-55

CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Oxyphenylbutazone (I) [129-20-4] was oxidized when incubated with acetone powder prepared from sheep vesicular gland microsomes or with lipoxigenase [9029-60-1] at pH 4 or 5. Oxidation also occurred at pH 8 or 9, if arachidonate or linoleate was added to either of the incubation mixts. The oxygenated product was found to be identical with 4-hydroxyoxyphenbutazone [55648-39-0], which was synthesized and analyzed by gas liquid chromatog. and mass spectrometry. The oxygenated compound was not an inhibitor of prostaglandin biosynthesis.

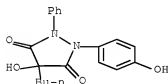
IT 55648-39-0

RL: FORM (Formation, nonpreparative)

(formation of, from oxyphenbutazone, by lipoxigenase and seminal vesicle microsomes)

RN 55648-39-0 HCAPLUS

CN 3,5-Pyrazolidinedione, 4-butyl-4-hydroxy-1-(4-hydroxyphenyl)-2-phenyl-  
(CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD  
(6 CITINGS)



## SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 16:19:09 ON 22 JAN 2010)

FILE 'HCAPLUS' ENTERED AT 16:19:17 ON 22 JAN 2010

E DEKKERS DAVID WALTERUS/AU

L1 12 SEA ABB=ON ("DEKKERS DAVE W C"/AU OR "DEKKERS DAVID W C"/AU  
OR "DEKKERS DAVID WALTERUS"/AU OR "DEKKERS DAVID WALTERUS  
CORNELIS"/AU)  
E AARDEN LUCIEN/AU

L2 164 SEA ABB=ON ("AARDEN L A"/AU OR "AARDEN LUCIAN A"/AU OR  
"AARDEN LUCIEN"/AU OR "AARDEN LUCIEN A"/AU OR "AARDEN LUCIEN  
ADRIANUS"/AU)  
E TENBRINKE JANNA ALBERDINA/AU  
E TENBRINK JANNA/AU

L3 25 SEA ABB=ON "TENBRINK J"/AU

L4 0 SEA ABB=ON L1 AND L2 AND L3

L5 173 SEA ABB=ON L1 OR L2

L6 3 SEA ABB=ON L5 AND ?PHENBUTAZON?  
SELECT RN L6 2

FILE 'REGISTRY' ENTERED AT 16:20:58 ON 22 JAN 2010

L7 5 SEA ABB=ON (129-20-4/BI OR 55648-39-0/BI OR 70-18-8/BI OR  
842163-84-2/BI OR 842163-85-3/BI)

FILE 'HCAPLUS' ENTERED AT 16:21:02 ON 22 JAN 2010

L8 3 SEA ABB=ON L6 AND L7

FILE 'REGISTRY' ENTERED AT 16:21:46 ON 22 JAN 2010

L9 STRUCTURE 55648-39-0

L10 0 SEA SSS SAM L9

L11 7 SEA SSS FUL L9

FILE 'HCAPLUS' ENTERED AT 16:22:56 ON 22 JAN 2010

L12 11 SEA ABB=ON L11

FILE HOME

FILE HCAPLUS

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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

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